Figures 1 and 2 Tuberculosis Testing and Diagnostic Notes
These notes are prepared to guide screening and medical evaluations for infants exposed to tuberculosis in Providence Hospital during the period September 2013 through August 16, 2014.

Information is based on recommendations from Heartland National TB Center, Curry International Tuberculosis Center, Centers for Disease Control and Prevention and the American Academy of Pediatrics.

Notes

1: Evaluation

- Ideally the CXR, TST, medical history and focused physical exam should all take place during the same clinic visit. It is not recommended to wait for (+) TST results before performing the rest of the evaluation.
- All TB contact screening and risk information can be collected using the Texas Department of State Health Services TB-208 form (Attachment 1).

2: Physical Exam

- The focused physical exam should capture temperature and growth parameters, alertness and meningeal signs, and the results of palpation of back and extremities. Special attention should be placed on the examination of the lungs and cervical lymph nodes.
- Lung findings are relatively modest; even if the infant has an abnormal CXR. Infants are most likely to have rales, decreased breath sounds, and increased work of breathing.

3: Symptoms

- TB symptoms in infants are often subtle or even absent. If TB disease (TBD) does occur, clinical manifestations most often appear 1 to 6 months after infection.
- The most common symptoms include weight loss/poor weight gain, fever, cough, chills, and night sweats.

4: Evaluation for TB Disease

- If an infant has TBD, they have metabolically active *M. tuberculosis* bacteria in some part of the body. Many infants are asymptomatic at the time of TB diagnosis.
- If TBD is suspected, diagnostic tests should be performed; gastric aspirates have the highest specimen yield for infants (see section on diagnostic tests in the American Academy of Pediatrics Red Book, 29th edition, page 739 for complete specimen collection information).
- It is difficult to confirm TB microbiologically as infants cannot easily produce sputa and sputa that are collected are usually smear (-). For concerns on specimen collection and lab submission, consult with the local health department or Texas Department of State Health Services.

- It is acceptable to over treat in uncertain situations. If a patient is not stable, specimens should be collected for cultures and treatment for TBD should be started; sometimes diagnosis becomes clear over time. If the diagnosis doesn't become certain, treatment for TBD should be completed. Weigh all likely diagnoses, consider risks and benefits, and make the best judgment after discussion with family and a pediatric TB physician-expert.
- Any diagnosis of TBD should be reported within 1 working day to the local health department or Texas Department of State Health Services.

Treatment

- The standard treatment for infants with TBD is a four-drug regimen using directly observed therapy (DOT). DOT can take place at home, work, school, clinic, or other agreed-upon location. Medication administration should be by a non-family member. Using DOT can increase completion rates to 90%. **DOT will be provided by the local health department.**

Table1. Four-drug treatment

Drug	DAILY dose in mg/kg/day (max dose)	TWICE WEEKLY dose in mg/kg/day (max dose)
Isoniazid	10-15 (300 mg)*	20-30 (900 mg)
Rifampin	10-20 (600 mg)*	10-20 (600 mg)
Pyrazinamide	30-40 (2 grams)	50 (2 grams)
Ethambutol ɣ	15-25 (1 gram)	50 (2.5 grams)

* When using **both** INH and RIF DAILY, dose INH at 10 mg/kg/dose and RIF no more than 15 mg/kg

ɣ Consider risk and benefit of ethambutol in infants whose visual acuity cannot be monitored

- The total duration of therapy is six months, and is measured by the number of observed doses. Infants receiving a typical regimen receive 40 daily doses in 8 weeks for completion of initiation phase; the continuation phase totals 90 doses in 18 weeks for 5 days per week dosing or 36 doses for twice-weekly dosing. During the initiation phase of treatment (the first 2 months of therapy), all four drugs are administered, usually daily administration. Ethambutol can be stopped once it is determined the patient or source case isolate is INH and RIF susceptible. At two months after starting therapy, repeat the CXR and assess the situation. If the infant is doing well: 1) gaining weight and not worsening clinically or radiographically, 2) taking and retaining each DOT dose, 3) absorbing the drugs and no concern for drug resistance exists, they can progress to the next phase of therapy. In the continuation phase, the infant receives 4 months of INH and RIF (if INH and RIF susceptible) by DOT 2 to 3 times weekly. Twice weekly DOT would amount to 36 doses in 18 weeks; three times weekly DOT would amount to 54 doses in 18 weeks.

- **Dosing** can be complicated and must be individualized for each patient; anticipate a trial-and-error period for 1 to 2 weeks at the beginning of therapy. Possible vehicles for medication include maple syrup, chili, Nutella, spinach baby food and chocolate whipped cream. The vehicle and drug can be layered on a spoon; the infant should be taught to take contents of the spoon without chewing.

Strategies may not work for every dose, be prepared to try new tricks. Never let the infant think the dose is optional.

- Though the typical course of treatment lasts 6 months there are situations where it can be prolonged: if disease is extensive or slow to respond, if the TB isolate is drug-resistant, or if patient has been poorly adherent, for example. If the infant has TB meningitis or osteomyelitis they will be treated for at least 12 months.

5: Radiology

- Two-view CXR is required: PA and lateral. Using two-views helps to identify the common abnormality: intrathoracic lymphadenopathy. Radiographic changes are common in pediatric TB and include intrathoracic lymphadenopathy and calcified granulomata. There is often a relative paucity of TB symptoms in comparison to radiographic changes.
- The radiology order form should include TB symptoms (if present) and the possibility of TB (i.e., this infant is a contact to an infectious TB case). Same-day interpretation should be requested from a radiologist who is experienced with pediatric TB.
- It is difficult to distinguish community-acquired pneumonia or asthma from TB based on radiographic findings.

6: TST

- A negative TST never rules out TBD; 20% of culture-proven pediatric TB cases are TST (-) when initially evaluated. Conversely, not every (+) TST indicates TB infection (TBI) or TBD. TST results should be weighed in context of immune status, CXR findings, medical history, physical examination results, and presence of symptoms. In more complex cases, a consult with a pediatric TB physician-expert is necessary.

7: TB Infection (TBI)

- If an infant has TBI, the organism is dormant. Both the physical examination and the radiograph will be normal, but the TST will be positive (in this situation ≥ 5mm). It is important to treat all infants who have TBI, as infants are more likely to develop TB once infected than are adults. Infants with TBI are recent infections (in this situation, all infections would be presumed to be due to exposure since September 2013), which increases the risk that they will progress to TBD. Infants may develop TBD within weeks of infection.
- If an infant tests TST (+), begin a 9-month course of INH for TBI. If dosed 5 days per week (10-15 mg/kg/day, maximum dose of 300 mg) this should equate to at least 270 doses; the goal is to finish 270 doses within 12 months. A twice weekly regimen is acceptable with INH 20-30 mg/kg/day (maximum dose 900 mg); this would amount to 76 total doses in 38 weeks. Practitioners should be mindful of gastro-intestinal side effects associated with INH syrup and work with the parent to minimize these effects. Should drug sensitivity tests reveal that the index is INH-resistant, RIF can be used to treat TBI. RIF can be given 5 days per week at 10-20 mg/kg/day (maximum dose 600 mg) for 6 months. TBI treatment is less toxic in infants than in adults. All confirmed and suspected cases should be reported to the local health department or Texas Department of State Health Services within one working day.

- Families must be educated on what to expect throughout TBI therapy. They should understand symptoms of drug toxicity and the importance of treatment adherence. Infants should be seen monthly during the course of treatment. Quick nurse visits can be used to ensure adherence to therapy, monitor for toxicity, and dispense medication. Directly observed therapy (DOT) is the standard of care for infants with TBI.
- Liver function testing (LFT) is no longer standard; most infants tolerate therapy well. LFTs are recommended for infants with underlying liver disease, who are taking other hepatotoxic meds, or who have symptoms of hepatotoxicity.
- Infants should be watched for anorexia, malaise, and/or abdominal pain; the family should stop treatment and contact the LHD right away if symptoms develop.
- Vitamin B6 (pyridoxine) can be prescribed in addition to INH in certain circumstances, such as for infants who have underlying health problems, poor diets or who feed poorly, or who are breastfed. The tablets can be crushed or fragmented into liquid or soft vehicles.

Table 2. B6 daily dosing in children

Age of infant	B6 dose	
Infant	6.25 mg	¼ of 25 mg tablet
Toddler	12.5 mg	½ of 25 mg tablet
School-aged	25 mg	25 mg tablet

8: Window Prophylaxis

- Since TST results are not reliable under the age of 6 months, any infant under 6 months of age who tests TST (-) on initial evaluation should receive window prophylaxis with INH. If dosed 5 days per week: 10-15 mg/kg/day (maximum dose of 300 mg). If dosed twice weekly: 20-30 mg/kg/day (maximum dose 900 mg).
- When they reach 6 months of age they should be tested again using TST. If the TST is still (-), the infant is immunocompetent, and there are no new TB symptoms, INH window prophylaxis can be stopped. If the second TST is (+), complete 9 months INH (the months of window prophylaxis **do** count into the 9 month total).
- If, during the course of TBI treatment, the infant is exposed to another adult with TBD, the evaluation should be repeated and the treatment should be extended.

Additional information: Bacille Calmette-Guerin (BCG) vaccine

- The bacille Calmette-Guerin (BCG) vaccine is routinely given to newborns in most areas of the world, including Mexico. BCG vaccine is not routinely given to newborns in the United States.
- BCG history should be ignored when placing or interpreting TST. However, an increased risk of positive TST results exists.